

FORM PTO-1449

INFORMATION DISCLOSURE STATEMENT

ATTY. DOCKET NO.
0942.4190002APPLICATION NO.
09/390,634APPLICANT
PRICE *et al.*FILING DATE
September 7, 1999GROUP
1651/633

U.S. PATENT DOCUMENTS

| EXAMINER INITIAL | | DOCUMENT NUMBER | DATE | NAME | CLASS | SUB-CLASS | FILING DATE |
|---------------------|-----|-----------------|------------|-------------------------|-------|-----------|-------------|
| <i>gk</i> | AA1 | 4,673,649 | 06/16/1987 | Boyce <i>et al.</i> | 435 | 240 | 07/15/1983 |
| <i>gk</i> | AB1 | 4,767,704 | 08/30/1988 | Cleveland <i>et al.</i> | 435 | 68 | 10/07/1983 |
| <i>gk</i> | AC1 | 4,927,762 | 05/22/1990 | Darfler, F.J. | 435 | 240.31 | 11/30/1988 |
| <i>gk</i> | AD1 | 4,940,666 | 07/10/1990 | Boyce <i>et al.</i> | 435 | 240.2 | 12/09/1986 |
| <i>gk</i> | AE1 | 5,024,947 | 06/18/1991 | Inlow <i>et al.</i> | 435 | 240.31 | 07/24/1987 |
| <i>gk</i> | AF1 | 5,045,454 | 09/03/1991 | Bertheussen, K. | 435 | 29 | 02/23/1990 |
| <i>gk</i> | AG1 | 5,063,157 | 11/05/1991 | Stockinger, H. | 435 | 240.2 | 01/11/1989 |
| <i>gk</i> | AH1 | 5,122,469 | 06/16/1992 | Mather <i>et al.</i> | 435 | 240.2 | 10/03/1990 |
| <i>gk</i> | AI1 | 5,187,077 | 02/16/1993 | Gearing <i>et al.</i> | 435 | 69.1 | 12/09/1988 |
| <i>gk</i> | AJ1 | 5,316,938 | 05/31/1994 | Keen <i>et al.</i> | 435 | 240.31 | 12/18/1992 |
| <i>gk</i> | AK1 | 5,322,775 | 06/21/1994 | Clark <i>et al.</i> | 435 | 69.1 | 11/22/1991 |

FOREIGN PATENT DOCUMENTS

| EXAMINER INITIAL | | DOCUMENT NUMBER | DATE | COUNTRY | CLASS | SUB-CLASS | TRANSLATION |
|---------------------|-----|-----------------|------------|---------|-------|-----------|-------------|
| <i>gk</i> | AL1 | WO 92/05246 | 04/01/1992 | WIPO | | | Yes No |
| <i>gk</i> | AM1 | WO 95/06716 | 03/09/1995 | WIPO | | | Yes No |
| <i>gk</i> | AN1 | WO 95/28412 | 10/26/1995 | WIPO | | | Yes No |
| <i>gk</i> | AO1 | WO 96/19245 | 06/27/1996 | WIPO | | | Yes No |
| <i>gk</i> | AP1 | WO 96/22362 | 07/25/1996 | WIPO | | | Yes No |

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

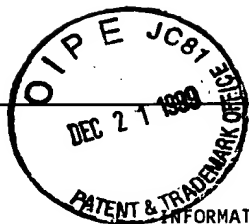
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| <i>gk</i> | AR | 1 | Abbondanzo, S.J. <i>et al.</i> , "Derivation of Embryonic Stem Cell Lines," <i>Meth. Enzym.</i> 225:803-822 (1993). |
| <i>gk</i> | AS | 1 | Baringa, M., "Knockout Mice: Round Two," <i>Science</i> 265:26-28 (1994). |
| <i>gk</i> | AT | 1 | Brûlet, P. <i>et al.</i> , "Monoclonal antibodies against trophectoderm-specific markers during mouse blastocyst formation," <i>Proc. Natl. Acad. Sci. USA</i> 77:4113-4117 (1980). |

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Joe Wautsch



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| EXAMINER INITIAL | | DOCUMENT NUMBER | DATE | NAME | CLASS | SUB-CLASS | FILING DATE |
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| <i>sk</i> | AA2 | 5,332,672 | 07/26/1994 | Conover, J. <i>et al.</i> | 435 | 240.2 | 04/09/1992 |
| | AB2 | 5,342,777 | 08/30/1994 | Cole <i>et al.</i> | 435 | 240.31 | 03/03/1992 |
| | AC2 | 5,405,772 | 04/11/1995 | Ponting | 435 | 240.31 | 06/18/1993 |
| | AD2 | 5,453,357 | 09/226/1995 | Hogan, B. | 435 | 7.21 | 10/08/1992 |
| | AE2 | 5,474,931 | 12/12/1995 | DiSorbo <i>et al.</i> | 435 | 240.31 | 09/21/1993 |
| | AF2 | 5,573,937 | 11/12/1996 | Shinmoto <i>et al.</i> | 435 | 240.1 | 01/09/1995 |
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| <i>sk</i> | AL2 | WO 96/22364 | 07/25/1996 | WIPO | | | Yes No |
| | AM2 | WO 96/39487 | 12/12/1996 | WIPO | | | Yes No |
| | AN2 | WO 97/33978 | 09/18/1997 | WIPO | | | Yes No |
| | AO2 | WO 97/34999 | 09/25/1997 | WIPO | | | Yes No |
| | AP | | | | | | Yes No |

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

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| <i>sk</i> | AR | 2 | Camper, S.A. <i>et al.</i> , "Implementing Transgenic and Embryonic Stem Cell Technology to Study Gene Expression, Cell-Cell Interactions and Gene Function," <i>Biology of Reproduction</i> 52:246-257 (1995). |
| | AS | 2 | Capecchi, M.R., "Altering the Genome by Homologous Recombination," <i>Science</i> 244:1288-1292 (1989). |
| | AT | 2 | Conover, J.C. <i>et al.</i> , "Ciliary neurotrophic factor maintains the pluripotentiality of embryonic stem cells," <i>Devel.</i> 119:559-565 (1993). |

EXAMINER *Paul M. Kerr*

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Joe W. W. W.



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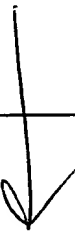

U.S. PATENT DOCUMENTS

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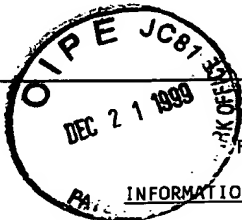
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|  | AR | <u>3</u> | Dinsmore, J. <i>et al.</i> , "Embryonic Stem Cells Differentiated <i>In Vitro</i> as a Novel Source of Cells for Transplantation," <i>Cell Transpl.</i> 5:131-143 (March/April 1996). |
|  | AS | <u>3</u> | Doetschman, T. <i>et al.</i> , "The <i>in vitro</i> development of blastocyst-derived embryonic stem cell lines: formation of visceral yolk sac, blood islands and myocardium, <i>J. Embryol. Exp. Morph.</i> 87:27-45 (1985). |
|  | AT | <u>3</u> | Doetschman, T. <i>et al.</i> , "Establishment of Hamster Blastocyst-Derived Embryonic Stem (ES) Cells," <i>Dev. Biol.</i> 127:224-227 (1988). |

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| | APPLICANT PRICE <i>et al.</i> | |
| | FILING DATE September 7, 1999 | GROUP 1651 1633 |



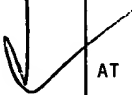
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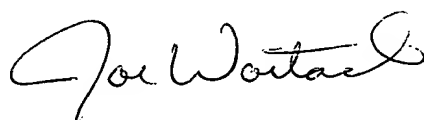
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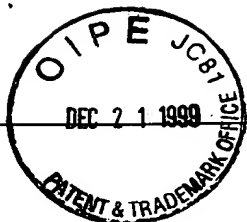
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|  | AR | <u>4</u> | Doetschman, T. <i>et al.</i> , "Embryonic Stem Cell Model Systems for Vascular Morphogenesis and Cardiac Disorders," <i>Hypertension</i> 22:618-629 (1993). |
|  | AS | <u>4</u> | Du, F. <i>et al.</i> , "Nuclear transfer of putative rabbit embryonic stem cells leads to normal blastocyst development," <i>J. Reprod. Fertil.</i> 104:219-223 (1995). |
|  | AT | <u>4</u> | Evans, M.J. and Kaufman, M.H., "Establishment in culture of pluripotential cells from mouse embryos," <i>Nature</i> 292:154-156 (1981). |

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September 7, 1999GROUP
1651

U.S. PATENT DOCUMENTS

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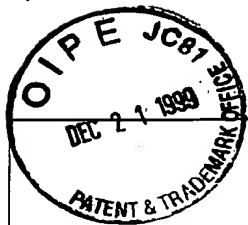
OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

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| | AR | <u>5</u> | Freshney, R.I., "Culture of Animal Cells," <i>A Manual of Basic Technique</i> , Alan R. Liss, Inc., publ., New York, pp.80-81 (1987). |
| | AS | <u>5</u> | Fry, R.C., "The Effect of Leukemia Inhibitory Factor (LIF) on Embryogenesis," <i>Reprod. Fertil. Dev.</i> 4:449-458 (1992). |
| | AT | <u>5</u> | Fuller, S.J. and Chien, K.R., "Genetic Engineering of Cardiac Muscle Cells: <i>In Vitro</i> and <i>In Vivo</i> ," in: <i>Genetic Engineering: Principles and Methods</i> , Vol. 16, Setlo, J.K., ed., Plenum Press, New York, pp. 17-31 (1994). |

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U.S. PATENT DOCUMENTS

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| <i>sk</i> | AR | <u>6</u> | <i>gw</i> GIBCO BRL Catalog, pp. 123-142, 145, 148, 153 (1992). |
| | AS | <u>6</u> | Gossler, A. <i>et al.</i> , "Transgenesis by means of blastocyst-derived embryonic stem cell lines," <i>Proc. Natl. Acad. Sci. U.S.A.</i> 83:9065-9069 (1986). |
| | AT | <u>6</u> | Graves, K.H. and Moreadith, R.W., "Derivation and Characterization of Putative Pluripotent Embryonic Stem Cells From Pre-Implantation Rabbit Embryos," <i>Molec. Reprod. Dev.</i> 36:424-433 (1993). |

EXAMINER

Paul M. Kerr

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Joe Wotack

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PATENT & INFORMATION DISCLOSURE STATEMENT


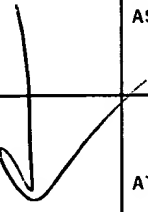
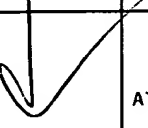
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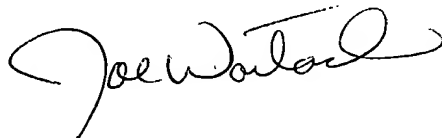
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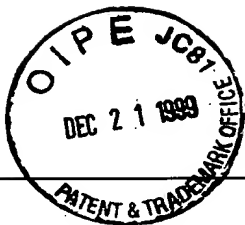
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|  | AR | Z | Gu, H. <i>et al.</i> , "Deletion of a DNA Polymerase β Gene Segment in T Cells Using Cell Type-Specific Gene Targeting," <i>Science</i> 265:103-106 (1994). |
|  | AS | Z | Ham, R.G., "Clonal Growth of Mammalian Cells in a Chemically Defined, Synthetic Medium," <i>Proc. Natl. Acad. Sci.</i> 53:288-293 (February 1965). |
|  | AT | Z | Ham, R.G., "Formulation of Basal Nutrient Media," <i>Methods for Preparation of Media, Supplements, and Substrata for Serum-Free Animal Cell Culture</i> , Alan R. Liss, Inc., publ., New York, pp. 3-21 (1984). |

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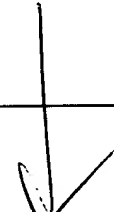

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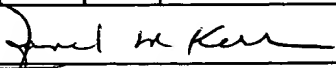
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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

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|  | AR | <u>8</u> | Hata, R.-I. and Senoo, H., "L-Ascorbic Acid 2-Phosphate Stimulates Collagen Accumulation, Cell Proliferation, and Formation of a Three-Dimensional Tissue-like Substance by Skin Fibroblasts," <i>J. Cell. Phys.</i> 138:8-16 (1989). |
|  | AS | <u>8</u> | "Isolation, Culture, and Manipulation of ES Cells," in <i>Manipulating the Mouse Embryo. A Laboratory Manual</i> , 2 nd Ed., Hogan, B. <i>et al.</i> , eds., Cold Spring Harbor Laboratory Press, pp. 255-258 (1994). |
|  | AT | <u>8</u> | Hollands, P., "Embryonic stem cell grafting: the therapy of the future?," <i>Human Reproduction</i> 6:79-84 (1991). |

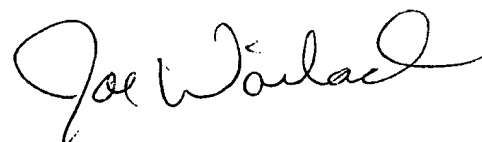
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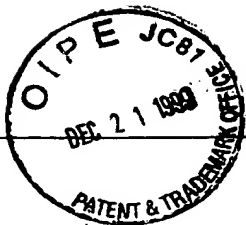


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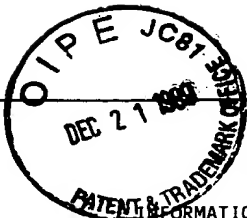
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| <i>jk</i> | AR | <u>2</u> | Hooper, M. <i>et al.</i> , "HPRT-deficient (Lesh-Nyhan) mouse embryos derived from germ line colonization by cultured cells," <i>Nature</i> 326:292-295 (1987). |
| <i>↓</i> | AS | <u>2</u> | Iannaccone, P.M. <i>et al.</i> , "Pluripotent Embryonic Stem Cells from the Rat Are Capable of Producing Chimeras," <i>Dev. Biol.</i> 163:228-292 (1994). |
| <i>↓</i> | AT | <u>2</u> | Keller, G. <i>et al.</i> , "Hematopoietic Commitment during Embryonic Stem Cell Differentiation in Culture," <i>Mol. Cell. Biol.</i> 13:473-486 (1993). |

EXAMINER *James H. Kerr*DATE CONSIDERED *3/4/00*

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Joe W. Wooten



FORM PTO-1449

PATENT INFORMATION DISCLOSURE STATEMENT

ATTY. DOCKET NO.
0942.4190002APPLICATION NO.
09/390,634APPLICANT
PRICE *et al.*FILING DATE
September 7, 1999GROUP
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U.S. PATENT DOCUMENTS

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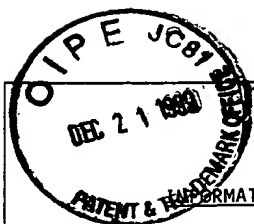
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| | AR | <u>10</u> | Johansson, B.M. and Wiles, M.V., "Evidence for Involvement of Activin A and Bone Morphogenetic Protein 4 in Mammalian Mesoderm and Hematopoietic Development," <i>Molec. Cell. Biol.</i> 15:141-151 (1995). |
| | AS | <u>10</u> | Keller, G.M., "In vitro differentiation of embryonic stem cells," <i>Curr. Opin. Cell Biol.</i> 7:862-869 (1995). |
| | AT | <u>10</u> | Lamb, B.T. <i>et al.</i> "Introduction and expression of the 400 kilobase precursor amyloid protein gene in transgenic mice," <i>Nature Genetics</i> 5:22-29 (1993). |

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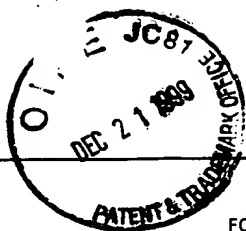
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| | AR | <u>11</u> | Lambert, K.J. and Birch, J.R., "Cell Growth Media," in: <i>Animal Cell Biotechnology Vol. 1</i> , Spier, R.E. and Griffiths, J.B., eds., Academic Press, pp. 85-123 (1985). |
| | AS | <u>11</u> | Loo, D.T. <i>et al.</i> , "Extended Culture of Mouse Embryo Cells Without Senescence: Inhibition by Serum," <i>Science</i> 236:200-202 (1987). |
| | AT | <u>11</u> | Maciag, T. <i>et al.</i> , "An Endocrine Approach to the Control of Epidermal Growth: Serum-Free Cultivation of Human Keratinocytes," <i>Science</i> 211:1452-1454 (1981). |

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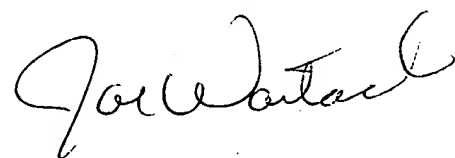
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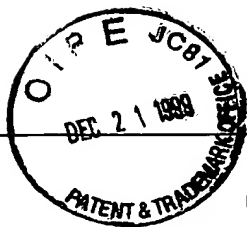
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|  | AR | 24 | Cost estimate, facsimile transmission from Anne Latour to Dr. Mindy Goldsborough, 2 pages, dated more than one year prior to January 10, 1997. |
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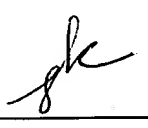
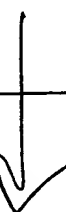

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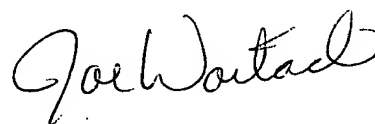
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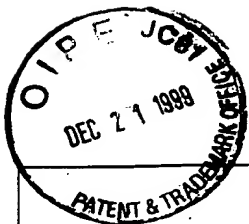
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|  | AR | 13 | Merlino, G.T., "Transgenic animals in biomedical research," <i>FASEB J.</i> 5:2996-3001 (1991). |
|  | AS | 13 | Nagy, A. <i>et al.</i> , "Derivation of completely cell culture-derived mice from early-passage embryonic stem cells," <i>Proc. Natl. Acad. Sci. USA</i> 90:8424-8428 (1993). |
|  | AT | 13 | Nakano, T. <i>et al.</i> , "Generation of Lymphohematopoietic Cells from Embryonic Stem Cells in Culture," <i>Science</i> 265:1098-1101 (1994). |

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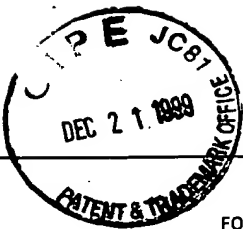
OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

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| <i>gk</i> | AR | <u>14</u> | Palacios, R. <i>et al.</i> , "In vitro generation of hematopoietic stem cells from an embryonic stem cell line," <i>Proc. Natl. Acad. Sci. USA</i> 92:7530-7534 (1995). |
| | AS | <u>14</u> | <i>PCT Gazette</i> , International Bureau of the World Intellectual Property Organization Under the Patent Cooperation Treaty, publ., p. 275 (January 1998). |
| | AT | <u>14</u> | Pease, S. <i>et al.</i> , "Isolation of Embryonic Stem (ES) Cells in Media Supplemented with Recombinant Leukemia Inhibitory Factor (LIF)," <i>Devel. Biol.</i> 141:344-352 (1990). |

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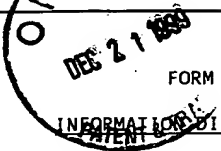
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| | AR | <u>15</u> 1 | Pederson, R.A., "Studies of <i>in vitro</i> Differentiation with Embryonic Stem Cells," <i>Reprod. Fertil. Dev.</i> 6:543-552 (1994). |
| | AS | <u>15</u> | Petters, R.M., "Transgenic Livestock as Genetic Models of Human Disease," <i>Reprod. Fertil. Dev.</i> 6:643-645 (1994). |
| | AT | <u>15</u> | Ray, W.J. and Gottlieb, D.I. "Regulation of Protein Abundance in Pluripotent Cells Undergoing Commitment to the Neural Lineage," <i>J. Cell. Physiol.</i> 168:264-275 (August 1996). |

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| | APPLICANT PRICE <i>et al.</i> | |
| | FILING DATE September 7, 1999 | GROUP 1651 1633 |


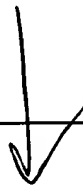
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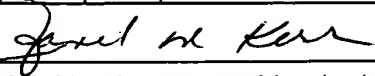
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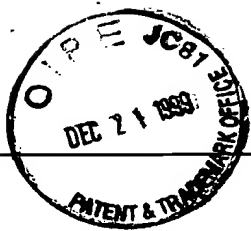
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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

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|  | AR | 16 | Robertson, E.J. <i>et al.</i> "X-chromosome instability in pluripotent stem cell lines derived from parthenogenetic embryos," <i>J. Embryol. Exp. Morph.</i> 74:297-309 (1983). |
|  | AS | 16 | Robertson, E. <i>et al.</i> , "Germ-line transmission of genes introduced into cultured pluripotent cells by retroviral vector," <i>Nature</i> 323:445-448 (1986). |
| | AT | 16 | Rose, T.M. <i>et al.</i> , "Oncostatin M (OSM) Inhibits the Differentiation of Pluripotent Embryonic Stem Cells <i>In Vitro</i> ," <i>Cytokine</i> 6:48-45 (1994). |

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Joe Whitad



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| gk | AR | 17 | Sigma Catalog, pp. 1510-1515, 1518-1529 (1994). |
| ↓ | AS | 17 | Shastry, B.S., "Genetic knockouts in mice: an update," <i>Experientia</i> 51:1028-1039 (1995). |
| ↓ | AT | 17 | Shuman, R.M., "Production of transgenic birds," <i>Experientia</i> 47:897-905 (1991). |

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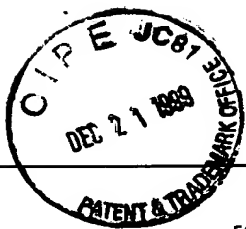
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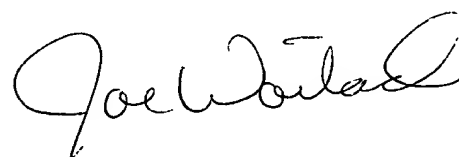
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| gk | AR | 18 | Smith, A.G. <i>et al.</i> , "Inhibition of pluripotential embryonic stem cell differentiation by purified polypeptides," <i>Nature</i> 336:688-670 (1988). |
| ↓ | AS | 18 | Smithies, O. and Maeda, N., "Gene targeting approaches to complex genetic diseases: Atherosclerosis and essential hypertension," <i>Proc. Natl. Acad. Sci. USA</i> 92:5266-5272 (1995). |
| ↓ | AT | 18 | Smithies, O., "Animal models of human genetic diseases," <i>Trends in Genetics</i> 9:112-116 (1993). |

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| EXAMINER INITIAL | | DOCUMENT NUMBER | DATE | COUNTRY | CLASS | SUB-CLASS | TRANSLATION |
|---------------------|----|-----------------|------|---------|-------|-----------|-------------|
| | AL | | | | | | Yes No |
| | AM | | | | | | Yes No |
| | AN | | | | | | Yes No |
| | AO | | | | | | Yes No |
| | AP | | | | | | Yes No |

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

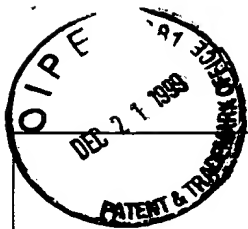
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| | AR | 19 | Snodgrass, H.R. <i>et al.</i> , "Embryonic Stem Cells and <i>In Vitro</i> Hematopoiesis," <i>J. Cell. Biochem.</i> 49:225-230 (1992). |
| | AS | 19 | Suda, Y. <i>et al.</i> , "Mouse Embryonic Stem Cells Exhibit Indefinite Proliferative Potential," <i>J. Cell. Phys.</i> 133:197-201 (1987). |
| | AT | 19 | Thompson, S. <i>et al.</i> , "Germ Line Transmission and Expression of a Corrected HPRT Gene Produced by Gene Targeting in Embryonic Stem Cells," <i>Cell</i> 56:313-321 (1989). |

EXAMINER

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3/4/00

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FORM PTO-1449

INFORMATION DISCLOSURE STATEMENT

ATTY. DOCKET NO.
0942.4190002APPLICATION NO.
09/390,634APPLICANT
PRICE *et al.*FILING DATE
September 7, 1999GROUP
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U.S. PATENT DOCUMENTS

| EXAMINER INITIAL | | DOCUMENT NUMBER | DATE | NAME | CLASS | SUB-CLASS | FILING DATE |
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| | AA | | | | | | |
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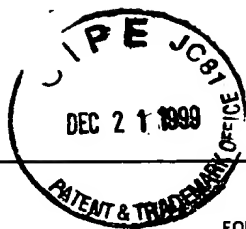
| | | | |
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| | AR | <u>20</u> | Thomson, J.A. <i>et al.</i> , "Isolation of a primate embryonic stem cell line," <i>Proc. Natl. Acad. Sci. USA</i> 92:7844-7848 (1995). |
| | AS | <u>20</u> | Wakamatsu, Y. <i>et al.</i> , "Establishment of a pluripotent cell line derived from a medaka (<i>Oryzias latipes</i>) blastula embryo," <i>Mol. Marine Biol. Biotech.</i> 3:185-191 (1994). |
| | AT | <u>20</u> | Wille, J.J. <i>et al.</i> , "Integrated Control of Growth and Differentiation of Normal Human Prokeratinocytes Cultured in Serum-Free Medium: Clonal Analysis, Growth Kinetics, and Cell Cycle Studies," <i>J. Cell. Physiol.</i> 121:31-44 (1984). |

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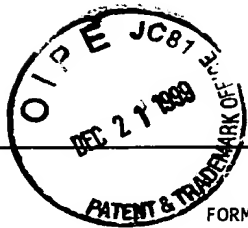
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| <i>gk</i> | AR | <u>21</u> | Wood, S.A. <i>et al.</i> , "Simple and efficient production of embryonic stem cell-embryo chimeras by coculture," <i>Proc. Natl. Acad. Sci. USA</i> 90:4582-4585 (1993). |
| | AS | <u>21</u> | Yagi, T. <i>et al.</i> , "A Novel ES Cell Line, TT2, With High Germline-Differentiating Potency," <i>Anal. Biochem.</i> 214:70-76 (1993). |
| | AT | <u>21</u> | Yanai, J. <i>et al.</i> , "Embryonic Cultures But Not Embryos Transplanted To The Mouse's Brain Grow Rapidly Without Immunosuppression," <i>Intern. J. Neuroscience</i> 81:21-26 (1995). |

EXAMINER *Paul H. Kerr*

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Joe W. Toland



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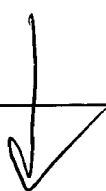

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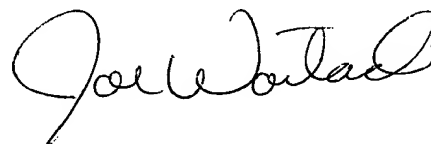
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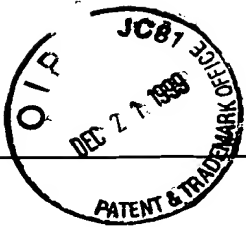
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|  | AR | <u>22</u> | Zang, M., <i>et al.</i> "Production of Recombinant Proteins in Chinese Hamster Ovary Cells Using A Protein-Free Cell Culture Medium," <i>Biotechnology</i> 13:389-392 (1995). |
|  | AS | <u>22</u> | Cost estimate, facsimile transmission from Dr. Mary Stevens to Dr. Mindy Goldsborough, 2 pages, dated more than one year prior to January 10, 1997. |
|  | AT | <u>22</u> | Reported data, facsimile transmission from Dr. Mary Stevens to Dr. Mindy Goldsborough, 5 pages, dated more than one year prior to January 10, 1997. |

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| <i>gk</i> | AR | <u>23</u> | Reported data, facsimile transmission from Dr. Mary Stevens to Dr. Mindy Goldsborough, Inc., 2 pages, dated more than one year prior to January 10, 1997. |
| | AS | <u>23</u> | Letter from Dr. Mindy Goldsborough to Dr. Mary Stevens, one page, dated less than 1 year prior to January 10, 1997. |
| | AT | <u>23</u> | Copy of letter from Dr. Mindy Goldsborough to Dr. Mary Stevens, signed by Dr. Mary Stevens, 1 page, dated less than one year prior to January 10, 1997. |

EXAMINER

David M. Kern

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3/4/00

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Joe Woulard

